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Title:	COMPOUNDS FOR THE NORMALIZATION OF THE SLEEP/WAKE CYCLE		

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APPELLANTS' REPLY BRIEF PURSUANT TO 37 C.F.R. § 41.41

In reply to the Examiner's Answer transmitted on April 2, 2010, and with reference to Appellants' Amended Appeal Brief filed on August 26, 2009, Appellants submit the following reply brief.

Summary

Claims 1-3, 5, 7-20, and 22-26 are pending and on appeal. Claims 4, 6, 21, and 27-30 have been cancelled. In the Examiner's Answer, the Examiner has maintained the rejection of the present claims on four grounds. Claims 1-3, 5, 7-20, and 22-26 stand rejected under 35 U.S.C. § 112, first paragraph, for lack of enablement. Claims 1, 12, 13, 17-20, 22, and 23 stand rejected under 35 U.S.C. § 112, second paragraph. Claims 1-3, 5, 7-20, and 22-26 stand further rejected for obviousness-type double patenting over claims 1-16 of U.S. Patent No. 6,103,703 (hereafter "Renshaw") and under 35 U.S.C. § 103 for obviousness over Renshaw.

As stated in Appellants' brief on appeal, the Examiner has failed to support these grounds of rejection properly.

Summary of Claimed Subject Matter

The application includes four independent claims, claims 1, 12, 17, and 22.

Independent claim 1 provides a method of normalizing the sleep/wake cycle of a mammal, the method including orally administering a therapeutically-effective amount of a

compound including cytidine, cytidine monophosphate (CMP), cytidine diphosphate (CDP), cytidine triphosphate (CTP), deoxycytidine monophosphate (dCMP), deoxycytidine diphosphate (dCDP), deoxycytidine triphosphate (dCTP), cytidine diphosphate-choline (CDP-choline), or cytosine, wherein the mammal is not suffering from insomnia (Specification, page 1, lines 27-30; page 2, lines 6-8; page 7, lines 24-27; and page 9, lines 16-18).

Independent claim 12 provides a method of treating a sleep disorder, the method including administering to a mammal a therapeutically-effective amount of a compound including cytidine, cytidine monophosphate (CMP), cytidine diphosphate (CDP), cytidine triphosphate (CTP), deoxycytidine monophosphate (dCMP), deoxycytidine diphosphate (dCDP), deoxycytidine triphosphate (dCTP), cytidine diphosphate-choline (CDP-choline), or cytosine, wherein the mammal's health is not compromised because of an existing physical condition and wherein the mammal is not suffering from insomnia (Specification, page 2, lines 3-8; page 5, lines 16-19; page 7, lines 24-27; and page 9, lines 16-18).

Independent claim 17 provides a method of increasing cognitive function in a sleep-deprived mammal, the method including administering a therapeutically-effective amount of a compound including cytidine, cytidine monophosphate (CMP), cytidine diphosphate (CDP), cytidine triphosphate (CTP), deoxycytidine monophosphate (dCMP), deoxycytidine diphosphate (dCDP), deoxycytidine triphosphate (dCTP), cytidine diphosphate-choline (CDP-choline), cytosine, creatine, adenosine, adenosine monophosphate (AMP), adenosine diphosphate (ADP), adenosine triphosphate (ATP), S-adenosylmethionine, propentofylline, or EHNA to a mammal suffering from sleep deprivation, wherein the mammal is not suffering from insomnia (Specification, page 2, lines 6-8; page 2, lines 11-14; page 7, lines 24-27; page 9, lines 1-7; and page 9, lines 16-18).

Independent claim 22 provides a method of treating a sleep disorder, the method including administering to a mammal in need thereof a therapeutically-effective amount of a compound including cytidine, cytidine monophosphate (CMP), cytidine diphosphate (CDP), cytidine triphosphate (CTP), deoxycytidine monophosphate (dCMP), deoxycytidine diphosphate (dCDP), deoxycytidine triphosphate (dCTP), cytidine diphosphate-choline (CDP-choline), cytosine, creatine, adenosine, adenosine monophosphate (AMP), adenosine diphosphate (ADP), adenosine triphosphate (ATP), S-adenosylmethionine, dipyridamole, propentofylline, or EHNA,

wherein the sleep disorder is not insomnia or sleep apnea (Specification, page 2, lines 3-8; page 7, lines 24-27; and page 9, lines 16-18).

New References Cited

Initially, Appellants note that the Examiner has relied on two new references in maintaining the rejections for indefiniteness, Taber's Cyclopedic Medical Dictionary, pg. 1653, and obviousness, The Merck Manual of Diagnosis and Therapy, 18th edition, pg. 1693. Neither reference is listed in section 8 on page 3of the Answer, neither reference has been provided to Appellants, and neither reference has been listed on a Form-892 supplied to the Appellants. Appellants request that copies of these references be provided and that the references be acknowledged on a Form-892 or that the references be removed as a basis of the rejection.

In addition, The Merck Manual of Diagnosis and Therapy, 18th edition was published in 2006, which is four years after the priority date of the present application. Accordingly, this reference is not prior art to the present application.

Disclaimer of Uridine and Related Compounds

After the brief was filed in this application, Appellants became aware of data that call into question the ability of cytidine to interconvert into uridine in vivo. Those data and related arguments were presented to the Office on February 22, 2010 in co-owned U.S. Application No. 11/629,111. As amendments are not allowed at this point in prosecution, Appellants have not amended the claims to disclaim uridine but will do so after a decision is rendered by the Board. For the purpose of this appeal, Appellants disclaim use of a compound comprising uridine, uridine monophosphate (UMP), uridine diphosphate (UDP), uridine triphosphate (UTP), and triacetyl uridine. Claims 3, 5, 7, 16, 18, and 26 are unaffected by this disclaimer.

Rejections under 35 U.S.C. 112, first paragraph

As previously argued, each of independent claims 1, 12, 17, and 22 is directed to treatment of a disorder or condition associated with sleep in specified classes of mammals by employing one of the listed classes of compounds.

The present invention is based on the discovery by the inventors that citicoline, i.e., CDP-choline, is useful for the normalization of the sleep/wake cycle and improves quality of sleep and

mood. The specification describes experiments performed by the inventors on human subjects at page 7, lines 1-4 and Figure 1 and page 7, lines 15-21 and Figures 2A and 2B. As is further noted in the specification, based on these experimental observations, it is reasonable to conclude that citicoline stabilizes homeostatic processes involved in numerous sleep disorders (Specification, page 6, lines 23-26) and may be used to increase cognitive functioning in subjects in a sleep-deprived state (Specification, page 6, line 26 – page 7, line 1).

The specification further teaches that citicoline is metabolized into cytidine and choline, thereby supporting the claimed use of this additional class of compounds (Specification, page 8, lines 3-7). The specification also teaches that adenosine-containing or elevating compounds may similarly be capable of maintaining sleep homeostasis and are accordingly useful in the claimed methods (Specification, page 8, lines 19-27). Finally, the specification teaches that creatine may be useful in the methods of the invention, as it increases levels of ATP (Specification, page 9, lines 22-25).

Moreover, the specification provides examples of specific compounds that may be employed in the claimed methods (Specification, pages 7-9) and describes exemplary doses, formulations, and routes of administration for these compounds (Specification, pages 9-11).

Accordingly, the specification provides experimental data and additional reasoning that would lead one skilled in the art to conclude that a compound comprising cytidine, cytidine monophosphate (CMP), cytidine diphosphate (CDP), cytidine triphosphate (CTP), deoxycytidine monophosphate (dCMP), deoxycytidine diphosphate (dCDP), deoxycytidine triphosphate (dCTP), cytidine diphosphate-choline (CDP-choline), cytosine, creatine, adenosine, adenosine monophosphate (AMP), adenosine diphosphate (ADP), adenosine triphosphate (ATP), S-adenosylmethionine, propentofylline, or erythro-9-(2-hydroxy-3-nonyl)adenine (EHNA) is effective in the claimed methods. Further, the specification provides a teaching with respect to administration of these compounds for these methods.

Thus, one skilled in the art, i.e., a medicinal chemist or physician, could practice the present invention without undue experimentation. And the scope of enablement is fully supported by sound scientific experiments – indeed, experimental data of human patients – and sound scientific reasoning. Appellants' full *Wands* analysis is provided in the brief at pages 11-20 and is not repeated here.

Appellants have identified several fundamental legal errors made by the Examiner in maintaining the rejection for lack of enablement in the Answer: (1) the rejection has no basis in law; (2) the rejection has no basis in fact; and (3) the rejection fails to consider the different limitations of the independent and dependent claims.

Basis in Law

As repeatedly argued, the Examiner is applying an incorrect legal standard for enablement of the present claims. In particular, while the Examiner has insisted that the present rejection is not a utility rejection, he has continued to rely on law and guidance that relates only to utility rejections (and corresponding rejections for lack of enablement on the basis of lack of utility). For example, the Examiner bases his position on M.P.E.P. §§ 2107.01(IV)-2107.04, which relate to utility rejections (Answer, page 10).

Moreover, the Examiner continues to rely on a *non-precedential* decision by the Board, *Ex parte Balzarini* (Answer, page 10), which the Examiner characterizes as "precedent that is clearly applicable." (Answer, page 12). The Examiner's characterization of the legal standing of this decision is, however, incorrect. This decision is not listed on the Office's website as one of the twenty-three precedential opinions, and it is therefore not binding on the Board or the Office. Accordingly, the Examiner's continued reliance on it to maintain the rejection is improper.[1]

In addition, the Examiner has repeatedly asserted that the standards for enablement of claims directed to medicinal treatment are different from the standard for other types of claims (Answer, page 10). The standard for enablement is, however, the same for all types of claims.

The Examiner also misinterprets the burdens of proof in making an enablement rejection. The Examiner states:

> Examiner is unaware of any legal requirement that arguments in support of the 112, first paragraph enablement requirement require scientific evidence of inoperability to support a rejection alleging lack of adequate enabling support. (Answer, page 12)

But this is not the correct standard to apply. As noted by Appellants, M.P.E.P. § 2164.04 requires:

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1 Appellants have previously noted the differences between the facts in the present case and those of *Ex parte Balzarini* in the brief at pages 10-11.

> A specification disclosure which contains a teaching of the manner and process of making and using an invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented *must* be taken as being in compliance with the enablement requirement ..., unless there is a reason to doubt the objective truth of the statements contained therein... (emphasis added)

Furthermore, the Office is required to "back up assertions of its own with acceptable evidence or reasoning which is *inconsistent* with the contested statement." (M.P.E.P. § 2164.04; emphasis added). In this case, the Examiner has provided no evidence or scientific reasoning that calls into question the statements made in the present specification.

Basis in Fact

Compounding the failure to support the present rejection on legal grounds, the Examiner appears to base the rejection on personal opinion. There are no facts provided on pages 3-5 or 9-18 of the Answer that would indicate that the specification is not enabling. Instead, only opinion is provided. For example, on page 17 of the Answer, the Examiner asserts that the statement "the Examiner had found that the claims were flawed because of the presence of both indefinite terms and functional terminology that adversely effected [sic] analysis of claim scope..." is a fact. This of course is pure opinion, and such conclusory statements are all that supports this rejection.

As previously argued, the basis for the rejection is the Examiner's unsupported belief that Appellants have not provided sufficient data to support the claimed scope. Most notably, the Examiner insists that such data are from a single subject and that they are insufficient. This belief is in error. In fact, the specification provides data from more than one subject, in contrast to the Examiner's assumption (Answer, page 16). With respect to the data in Figure 1, the specification states:

> Data in Figure 1 show that the administration of citicoline increases the quality of sleep and mood of human subjects, as measured by the subjects on a 10 point scale, compared to subjects receiving a placebo. (Specification, page 7, lines 1-4; emphasis added)

As the specification makes reference to multiple subjects, as opposed to a single subject, there is no basis for the Examiner to conclude that multiple subjects were not involved.

As is stated in the specification on page 7, Figure 1 shows data indicating that CDP-choline improves sleep quality, and Figures 2A-2B show the normalization of the sleep/wake cycle of a patient after administration of CDP-choline. The data in Figure 1 are on the quality of sleep for multiple subjects. Thus, the specification provides supporting data on the ability of CDP-choline to affect sleep for more than one individual, in contrast to the assertion of the Examiner. Figure 2A shows the activity levels of a subject over five days prior to administration of CDP-choline, and Figure 2B shows the activity levels of the same subject over five days after treatment with CDP-choline (Specification, page 7, lines 15-21). The specification further states that CDP-choline was effective in normalizing the sleep/wake cycle of the subject of Figures 2A-2B (Specification, page 7, lines 17-19). The Examiner dismisses such data because the subjects studied used cocaine. While Appellant agree that the subjects of the experiments represented in Figures 1 and 2A-2B were cocaine users, Appellants (who are experts in this field) have concluded that the results of CDP-choline on the sleep/wake cycle and quality of sleep are also applicable to individuals who are not users of cocaine. The Examiner has provided no facts or scientific reasoning to the contrary.

Limitations of the Claims

The rejection for lack of enablement also fails to consider the limitations of the individual claims. The four independent claims are directed to methods of normalizing the sleep/wake cycle, treating a sleep disorder, and increasing cognitive function in a sleep-deprived mammal. Throughout prosecution, the Examiner has grouped all claims together without regard to the specific subject matter recited. As the Examiner admits: "Although Examiner has not specifically addressed the term 'normalizing the sleep/wake cycle,' Examiner has repeatedly referred to the general subject matter of the instant claim set throughout the *Wands* analysis." (Answer, page 12). However, as stated by M.P.E.P. 2164: "The invention that one skilled in the art must be enabled to make and use is that defined by the claim(s) of the particular application or patent." Thus, the Examiner's consideration of only the general subject matter rather than the specific limitations of the claims is reversible error.

Moreover, in the brief, Appellants separately argued that additional considerations support the enablement of dependent claims 3, 5, 7, 9, 13, 16, 18, 23, and 26 (pages 19-20). In response to these arguments, the Examiner states only: "Beginning at page 19 of the Brief,

Appellant argues separately that certain dependent claims are separately enabled." (Answer, page 18). Appellants' arguments with respect to these claims are not addressed or disputed by the Examiner.

In short, a consideration of the *Wands* factors indicates that the instant claims are enabled. The claims are supported by human data and substantial guidance in the specification, and, as evidenced by the prior art, the claims are directed to known, tractable problems. As discussed above, the present rejection has no basis in law or in fact, and the Examiner has examined the claims on the basis of general subject matter rather than the specific limitations. Accordingly, the rejection should be reversed.

Rejections under 35 U.S.C. § 112, second paragraph

With respect to the rejections for indefiniteness, Appellants again submit that the claims are definite, as one skilled in the art would understand the metes and bounds of the claims. As argued, the purpose of the definiteness requirement is to ensure that "the scope of the claim is clear to a hypothetical person possessing the ordinary skill in the pertinent art" (M.P.E.P. § 2171). An applicant "can define in the claims what they regard as their invention essentially in whatever terms they choose... [and] may use functional language, alternative expressions, negative limitations, or any style of expression or format of claim which makes clear the boundaries of the subject matter for which protection is sought" (M.P.E.P. § 2173.01). In addition, "a claim may not be rejected solely because of the type of language used to define the subject matter for which patent protection is sought" (M.P.E.P. § 2173.01).

Appellants' reasoning in support of the definiteness of the claims is found on pages 20-28 of the brief on appeal. Appellants address each of the issues raised in the Answer at §§ 10.02-10.08 as follows.

§ 10.02 – Compound comprising

With respect to this rejection, Appellants have requested that the Examiner provide legal or factual support for his position. In reply, the Examiner has stated:

> "a compound comprising" is internally inconsistent because the term "a compound" is narrowly limited to single molecular species with well defined metes and bounds... while the term of art "comprising" ... implies that additional structural features are present in said "compound"...

While Appellants agree that a compound is a single molecular species, it does not follow that a compound cannot be described by reference to a key component part, as in the present claims. As previously argued, one skilled in the art would understand that a compound comprising cytidine includes compounds that formally include cytidine. As one skilled in the art would know whether a particular substance formally includes cytidine (or any of the other recited terms), the claims are definite. No argument by the Examiner addresses this point.

§ 10.03 – Physical condition

Appellants have previously argued that "physical condition" is a well-known term in the art and provided evidence of its usage in numerous scientific articles prior to the present priority date (Evidence Appendix G). In reply to these arguments, the Examiner has maintained the rejection because the entire term does not appear in the dictionaries at his disposal. The Examiner now bases the rejection on the definition of "physical" provided by two dictionaries and asserts that "physical condition" is indefinite because in his view there is more than one "agreed upon definition." In particular, based on the newly cited Taber's reference, the Examiner states that the term "physical" includes "medically relevant biochemical processes." According to the Examiner, Taber's, however, defines physical as "Concerning or pert. to the body, bodily." This definition does not use the term biochemical process, and the Examiner's position is simply not supported by the evidence.

Instead, as Appellants have argued, "physical condition" means any condition other than a mental condition. Both Stedman's and Taber's dictionaries are consistent with Appellants' position, and this rejection should be reversed.

§§ 10.04 and 10.05 – Substance abuse disorder

The Examiner has maintained the position that claim 13 broadens the scope of claim 12; this position is not understood. Claim 12 is directed to a "method of treating a sleep disorder." Claim 13 specifies that the sleep disorder is caused by a substance abuse disorder. Sleep

disorders may be caused by a substance abuse disorder or may not be caused by a substance abuse disorder. Accordingly, claim 13 limits claim 12 by excluding those sleep disorders not caused by substance abuse disorders. Claim 13 is narrower than (not broader than) claim 12 because it excludes certain sleep disorders. The same reasoning applies to the rejection of claim 23 in view of claim 22.

The Examiner also appears to be confused as to the meaning of a substance abuse disorder. The term has an art accepted meaning, for which Appellants have provided evidence (Evidence Appendix M). The term does not include overuse of any and all "substances," e.g., water and Fritos®, as alleged by the Examiner. The term is limited to disorders resulting from substances, e.g., alcohol, caffeine, and cocaine, whose abuse elicits a mental condition.

The Examiner also insists that the types of substance abuse disorders excluded by claim 19 are not defined with sufficient clarity. Appellants again note that claim 19 excludes *all* substance abuse disorders. Furthermore, as argued above, substance abuse disorder is a term known in the art. As the term is used consistent with it art known usage, claim 19 is definite. M.P.E.P. § 2173.05(i) confirms that this manner of claiming meets the requirements of 35 U.S.C. § 112, second paragraph, and this basis of the rejection should also be reversed.

§10.06 – Exclusion of insomnia

In the Answer, the Examiner asserts for the first time that the basis of this rejection is that:

> The treatment directed to "normalizing the sleep/wake cycle" appears to be overlapping with, and therefore inseparable from, a method of treatment of insomnia…
>
> ***
>
> [T]he instant claims have failed to avoid the overlap of "insomnia" with the asserted disease condition being treated.

This basis of rejection is also not understood. Claims 1, 12, 17, and 22 specifically exclude treatment of insomnia on their face. One skilled in the art reading these claims would readily understand this exclusion. There can be no more effective exclusion of subject matter than by stating that the methods do not include it. As with "substance abuse disorder" above, M.P.E.P. § 2173.05(i) confirms that Appellants may exclude subject matter from claims by use of a

negative limitation. Accordingly, the Examiner's position is without merit and should be reversed.

§10.07 - Preambles

The Examiner appears to reject each of the independent claims for indefiniteness because:

> The treatment appears to be solely directed to amelioration of the symptoms of drug addiction..., but does not appear to be directed to treatments leading to the normalization of the sleep/wake cycle, treating a sleep disorder, or increasing cognitive function in any non-addicted host.

Here, it appears that the Examiner has confused 35 U.S.C § 112, first paragraph with 35 U.S.C. § 112, second paragraph. As stated in M.P.E.P. § 2174, the requirements of § 112, first and second paragraphs, are separate and distinct, and the Examiner's position for this rejection does not indicate that one skilled in the art would not understand the metes and bounds of the claims.

The independent claims are directed to the subject matter recited on their faces, i.e., normalizing the sleep/wake cycle, treating a sleep disorder, and increasing cognitive function in a sleep-deprived mammal. The Examiner's dismissal of the human data in the specification as involving drug abusing hosts is not relevant to the definition of the terms in the claims. The preambles of the present claims use art accepted terminology and are thus readily understood by the skilled artisan (Evidence Appendices A, F, and K). Nothing more is required to meet the definiteness requirement. This basis of the rejection should also be reversed.

§10.08 – Problem Sleepiness

Appellants have previously argued and provided evidence that "problem sleepiness" is an art known term (Evidence Appendix B). In maintaining the rejection, the Examiner states:

> said [evidence provided by Appellant] is found to be of only incidental relevance to the instant claims, claims that are only enabled solely by exemplifications wherein the examiner, in an abundance of caution, must assume that the effects and/or side effects of cocaine addiction present in the tested hosts as the fundamental causative problem in each and every test subject...

As with §10.07, the Examiner has confused enablement with definiteness, which is improper (M.P.E.P. § 2174). As with the preambles of the claims, problem sleepiness is an art known term, and one skilled in the art would thus understand its meaning. This basis of the rejection should also be reversed.

Obviousness and Obviousness-type Double Patenting

The final basis of appeal is the rejection of all claims for both obviousness and obviousness-type double patenting over Renshaw. The analytical framework to be used in determining obviousness and obviousness-type double patenting was set forth by the U.S. Supreme Court in *Graham v. John Deere Co.*, 383 U.S. 1, 17-18, 148 USPQ 459 (1966):

> Under § 103, the scope and content of the prior art are to be determined; differences between the prior art and the claims at issue are to be ascertained; and the level of ordinary skill in the pertinent art resolved. Against this background, the obviousness or nonobviousness of the subject matter is determined. Such secondary considerations as commercial success, long felt but unsolved needs, failure of others, etc., might be utilized to give light to the circumstances surrounding the origin of the subject matter sought to be patented. As indicia of obviousness or nonobviousness, these inquiries may have relevance.

The Supreme Court reaffirmed this standard for obviousness in *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 82 USPQ2d 1385 (2007).

In order to support a *prima facie* case of obviousness the Examiner must make appropriate findings of fact and consider these facts in light of evidence provided by the Appellant. Furthermore, any obviousness rejection requires an analysis of the differences between the prior art and the claimed invention, as well as reasoning why one skilled in the art would bridge the gap between the two (M.P.E.P. § 2141(III)).

Appellants previously argued that an analysis of the *Graham* factors shows that the present claims are patentable over Renshaw and not obvious variants of the claims of Renshaw (Brief, pages 28-32). In response, the Examiner cites Renshaw in view of a new reference, the Merck Manual of Diagnosis and Therapy, page 1693. As the Merck Manual is newly cited, this brief represents Appellants' first opportunity to address it.

As previously argued, Renshaw is directed to methods of preventing or ameliorating a stimulant-induced disorder and cerebral vasoconstriction sequelae by administering a cytidine-

containing or cytosine-containing compound, such as CDP-choline (col. 1, line 53 – col. 2, line 10). Renshaw further states that cerebral vasoconstriction sequelae may include cognitive impairment (col. 3, ll. 22-29). Cocaine is one example of a stimulant. The reference is completely silent with respect to disruptions of the sleep/wake cycle, any sleep disorder, and any effects of sleep deprivation. In contrast to Renshaw, the present claims are directed to a method of normalizing the sleep/wake cycle of a mammal (claim 1); methods of treating a sleep disorder (claims 12 and 22), and a method for increasing cognitive function in a sleep-deprived mammal (claim 17). The claimed methods employ *inter alia* cytidine- or cytosine-containing compounds, such as CDP-choline. The sleep disorders treated may be caused by substance abuse disorders (e.g., claims 13, 14, 23, and 24) or not caused by substance abuse disorders (e.g., claim 19).

The significant differences between the prior art and the claimed invention are that Renshaw does not discuss sleep or sleep deprivation in any context, and there is nothing in Renshaw that connects stimulant use or cerebral vasoconstriction with disruptions in the sleep/wake cycle (claim 1), sleep disorders (claims 12 and 22), or cognitive impairment in sleep-deprived mammals (claim 17). Furthermore, claim 19 explicitly excludes treatment of a sleep disorder caused by substance abuse.

According to the Examiner, claims 5 and 6 of Renshaw are directed to treatment of stimulant-induced vasoconstriction sequelae, where the sequelae include "a vegetative response" or "motor activity impairment." The Examiner then asserts that taken together, these sequelae equate to "sleepiness." (Answer, page 23) Appellants disagree. The Examiner has provided no support for the position that a vegetative response or motor activity impairment are in any way connected to sleep.

The Examiner further asserts that the Merck Manual states that "withdrawal from heavy use [of cocaine] is characterized by somnolence...," which the Examiner also asserts means "sleepiness." (Answer, page 23). Based on this reference, the Examiner now asserts that Renshaw "is found to inherently include all of the instant treatment-directed subject matter as variations that would have been obvious to the ordinary practitioner..." (Answer, page 24). Appellants again disagree and again note that the Merck Manual, 18th edition, published in 2006, is not prior art to the present application.

As noted above, the Office has failed to provide any connection between "a vegetative response," "motor activity impairment," and sleep. Accordingly, there is no basis to conclude

that the treatment of these sequelae in Renshaw includes or overlaps with any of the claimed subject matter. With respect to somnolence as a symptom of withdrawal from heavy use of cocaine, the Examiner has asserted that somnolence is only a symptom of certain users of cocaine, i.e., some heavy users undergoing withdrawal. Not all users of cocaine exhibit this symptom. Renshaw also does not specifically discuss methods for treating individuals having somnolence or undergoing withdrawal from heavy cocaine use. As Renshaw does not specifically disclose treatment of sleep-related disorders, nor treat a population in which all members suffer from a sleep-related disorder, the reference cannot teach or suggest such treatment.

Appellants have noted that the Examiner supports the rejection, in part, by asserting that Renshaw inherently includes treatment of somnolence in cocaine users. As previously argued, the standard for obviousness is not whether a prior art reference includes or encompasses a particular treatment, but rather whether the treatment as claimed is obvious in view of the teachings of the reference. Appellants note that, under M.P.E.P. § 2112, inherent disclosure of an element is only present when that characteristic "is necessarily present in the thing described in the reference." As Renshaw does not discuss somnolence or any population that is necessarily suffering from somnolence, Renshaw cannot inherently teach the treatment of somnolence. Here, there is nothing in Renshaw (alone or in combination with the Merck Manual) that would suggest normalizing the sleep/wake cycle, treating a sleep disorder, or increasing cognitive function in a sleep-deprived mammal, because the references do not explicitly or inherently teach or suggest such uses.

Appellants again note that the Examiner has not properly considered the legal requirements for a rejection for obviousness. The entire basis of the rejections remains that "the instant claims and the claims of [Renshaw] have been correctly determined to be directed to overlapping subject matter." (Answer, page 24). Again, this position of the Examiner shows a lack of consideration of the scope of Renshaw, the scope of the present claims, and the differences between the two. The Examiner has also again made a general rejection of all claims without considering their individual limitations.

Further, the Examiner has failed to provide any legal support for the position that potential overlap alone is sufficient to establish a *prima facie* case of obviousness. While the methods of Renshaw are directed to treatment of individuals who may also be treated using the

methods of claims 1, 12, 17, and 22, the Examiner has provided no rationale as to why this potential overlap in patient populations would lead the skilled artisan to modify the teachings of Renshaw to arrive at the methods of any of independent claims 1, 12, 17, or 22. Appellants also note that as The Merck Manual, 18th edition, is not prior art, it cannot be the basis for a rationale to modify Renshaw. Furthermore, each of these independent claims is directed to distinct subject matter, each requiring a separate rationale to support the rejection. On the present record, there is no reason why such a skilled artisan would alter the methods of Renshaw to produce what it claimed.

In sum, the Examiner has based the present rejections on a standard of "overlap" rather than consideration of the *Graham* factors. Proper consideration of the *Graham* factors shows that there is no connection between the teachings of Renshaw and the distinct methods of claims 1, 12, 17, or 22. Thus, there is no rationale to support the rejection for obviousness, and it should be reversed.

In addition to the obviousness rejection over Renshaw, the Examiner has rejected the claims for obviousness-type double patenting over Renshaw. As previously argued at pages 31-32 of the brief, the analysis for a rejection for obviousness-type double patenting parallels that for a rejection under 35 U.S.C. § 103. All arguments with respect to the obviousness rejection therefore apply with equal force to the rejection for obviousness-type double patenting. This rejection should also be reversed.

Finally, as previously argued and not addressed by the Examiner (Brief, pages 30-32), claim 19 specifically excludes treatment of a disorder caused by substance abuse. This claim is by definition excluded by the subject matter disclosed in Renshaw, and the Examiner has failed to provide any support for the rejection of this claim.

Conclusion

Appellant respectfully requests that the rejection of claims 1-3, 5, 7-20, and 22-26 be reversed. If there are any charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

Date: 6/2/10

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